

A Method for the Study of the Circulation in the Dog Using a Mechanical Left Ventricle¹

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WHILE the contributions of the ventricles and the blood vessels to an observed response are difficult to separate, the Starling 'heart-lung preparation' made possible the study of the cardiac mechanism alone, by utilizing an artificially controlled vascular system. The reverse experiment, that of studying the reactions of the isolated vascular system to controlled cardiac or left ventricular function, has recently been attempted and preliminary experiments have been described (1). In these studies a variable pump permitting independent control of rate, output and ejection velocity has been substituted for the left ventricle in dogs.

Many investigators have diverted the total circulation through an artificial pump-oxygenator mechanism or a pump for replacement of one ventricle. With few exceptions these methods have been developed for the maintenance of an adequate blood flow while surgical procedures are performed within the heart, and have not been oriented towards the physiologic study of the circulation or its responses to controlled pump function. An approach in some respects similar to that described here was utilized by Gibbs (2) and Tainter (3) for the study of drugs and circulatory phenomena. The output of their apparatus was dependent upon return flow from the venous system. Complete separation of cardiac and peripheral vascular function was not achieved because alterations in venous return which were due to peripheral vascular phenomena affected the artificial heart output.

A heart pump system for physiologic studies should fulfill the following criteria: *a*) complete diversion of the circulation through the pump, *b*) independent controls of rate and stroke volume through and beyond the physiologic ranges, *c*) maintenance of constant output in the face of sudden or marked changes in peripheral resistance, *d*) maintenance of normal pulsatile pressures and flows and intact cardiovascular responses in the animal, and *e*) prevention of damage to circulating

red cells or serious alteration in the physical or chemical characteristics of the blood. The purpose of this paper is to describe the development of a standardized method which fulfills these criteria.

PRELIMINARY STUDIES

Earlier studies with a small diaphragm pump (1) defined the necessary characteristics of an instrument for use in the studies planned.

Clotting. Clotting was not a significant factor, although no animal was completely heparinized. Clotting did not occur in machined and polished methyl methacrylate ball valves (4) and a comparative study revealed that highly polished methyl methacrylate was the least clot promoting of several plastics (5).

Hemolysis. Hemochromogen studies (6) revealed variable degrees of hemolysis (table 1). The small surface area of the diaphragms, and consequently the large thrust necessary for the maintenance of an adequate output probably contributed to this effect.

Air Embolism. Initial experiments frequently terminated in ventricular fibrillation with minute air bubbles visible in the coronary arteries. The insertion of a simple methyl methacrylate chamber at a level above the pump on the output side successfully removed air bubbles entering the pump accidentally through the reservoir.

Output Control. A pump of this design can be greatly affected by changes in resistance. Small increases in pressure in the arterial system depressed the output. This inadequacy is explained by the inefficiency of a mechanical connection between the reciprocating drive and the diaphragms, stretching of the diaphragms and their small total area. Most of the animals in these preliminary experiments had low systemic arterial pressures because of inadequate pump output and large infusions were required to maintain the circulation.

THE PUMP

A new pump has proved satisfactory for the controlled physiologic studies originally contemplated. The present apparatus (figs. 1 and 2) is a

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TABLE 1. PLASMA HEMOCHROMAGEN DETERMINATIONS (6)*

Pump	Dog	Time on Pump (min.)	Plasma Hb Level (mg/100 cc)
1	2	30	15.8
		60	22.2
	5	0	32.0
		60	22.2
		90	24.0
	6	105	16.0
		0	7.5
		60	56.0
		120	32.0
	23	150	14.6
210		10.0	

* Normal less than 7.5 mg hemoglobin/100 cc plasma.

combination piston-diaphragm pump.² A piston, driven by a $\frac{1}{2}$ h.p. variable speed motor, reciprocates within a cylinder at a known stroke length which may be varied at will. The piston displaces oil and through this hydraulic medium moves a diaphragm alternately forward and backward. The diaphragm does no work, acting merely as a partition between the oil and the blood. It is made of Kel-F and is 12 inches in diameter. Because of the large surface area large stroke volumes may be obtained with only slight movements of the diaphragm, thereby minimizing turbulence and hemolysis (table 1). The pump head is machined from 3-inch thick methyl methacrylate. Ball check valves, the air-trap and the blood reservoir are also machined and polished methyl methacrylate. All connections are made with S-22 Tygon.

Pump rates are from 35 to 280 strokes/min. The stroke volume can be regulated accurately through a range of from zero to approximately 160 cc/stroke by regulation of the piston stroke length. The recommended output range of the pump is from 0.2 to 6.0 l/min. independent of the rate. Beyond this range, high pressures developing in the hydraulic medium may open a safety valve designed to prevent structural damage to the pump.

Initially, at high pump outputs, application of a resistance in the outflow tubing still produced a decrease in stroke volume. This decreased output with resistance applied was found to be the true calculated output, based on the volume of the pump head and the piston stroke length, whereas the increased stroke volume when output was unresisted was due to faulty seating of the outflow ball valve. Therefore, the outflow valve was spring-

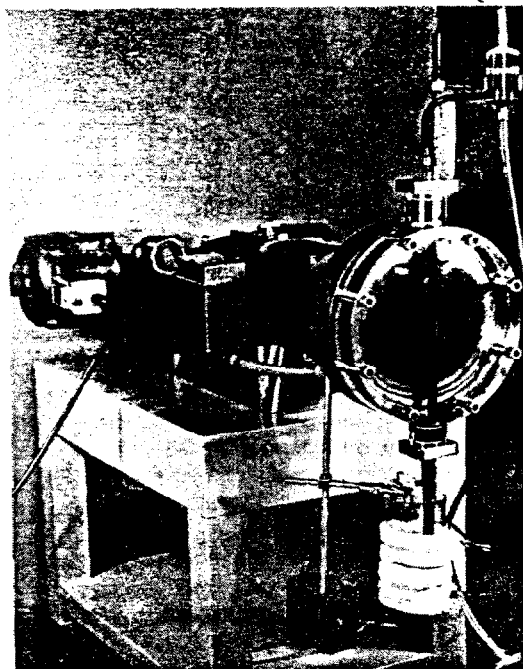


FIG. 1. Photograph of the present pump.

loaded with a highly polished stainless steel spring. The valve is so designed that the spring presents no obstacle to flow and has not produced clotting. With the spring-loaded valve stroke volumes remain constant over the entire range of outputs and rates even when as much as 500 mm Hg resistance is applied to the output tubing. High speed cinematography (64 frames/sec.) of both the inlet and outlet ball valves revealed firm seating with no chatter. No alteration in valve action occurred as increased resistance as high as 400 mm Hg was applied to the outlet tubing.

The total volume of the pump head and all connections, including a 5-inch level in the drainage reservoir is nearly 1 liter. The total volume of the previously described pump and all connections was less than 400 cc. The volume of the present apparatus makes the use of blood as a priming solution impractical. Five % purified gelatin in isotonic sodium chloride (Plazmoid)³ was found to be a suitable nontoxic primer (7). In several instances, the pump and connections were primed with mixtures of gelatin solution and blood. Through the transparent pump head the pseudo-agglutination, which has been reported with gelatin solutions (8), was visible, but when the solutions were warmed to 37°C before priming this phenomenon was not observed.

² Adapted from the 'Pulsafeeder' pump manufactured by Lapp Insulator Corporation, Le Roy, N. Y.

³ Generously supplied by Dr. E. L. Burbidge, Upjohn Company, Kalamazoo, Mich.

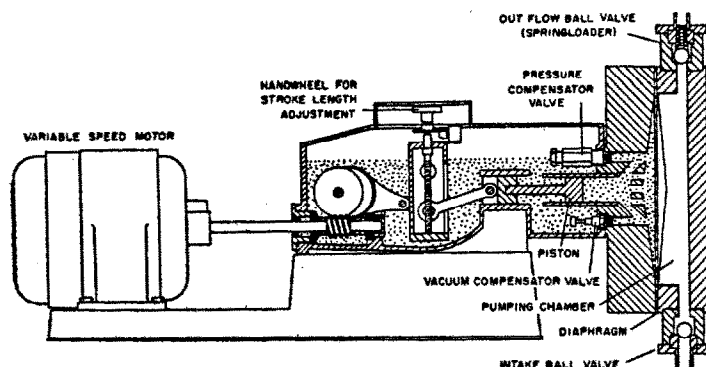


FIG. 2. Diagram to show mechanism of pump action. Stippled areas are oil-filled. See text for details.

Heating tapes⁴ composed of insulated wire are wrapped around the reservoir. The temperature of the blood in the reservoir is checked with a thermometer and maintained constantly at 37°C by regulating current flow with a variac.

PROCEDURE

The operative procedure includes placing a $\frac{3}{8}$ -inch i.d. methyl methacrylate T-tube in the descending arch of the aorta and a $\frac{3}{8}$ -inch i.d. S-22 Tygon drainage tube in the left auricle. Healthy mongrel dogs weighing 15–25 kg are anesthetized with Nembutal, 25 mg/kg body weight administered intravenously. The trachea is intubated. Following the usual surgical preparation, the chest is opened on the left side with a postero-lateral incision in the fifth interspace and respirations are maintained with oxygen under positive pressure. The ribs are retracted widely, the descending aorta is freed from its bed, and the first four pairs of intercostal arteries are ligated and divided. Two Potts noncrushing clamps are placed across the aorta for occlusion, one a few centimeters beyond the origin of the left subclavian artery and the other 6 centimeters distal to this. The aorta is almost completely divided midway between these two clamps. While the distal section of the aorta is held open with forceps a grooved limb of the aortic T-tube is gently manipulated into the vessel. A ligature is securely tied into the groove, holding the vessel wall securely to the plastic tube. The aorta is then sectioned completely and the proximal end intubated in the same manner. When secure, 5 mg of heparin in 20 cc of normal saline are allowed to flow through a length of Tygon tubing previously attached to the free limb of the T-tube so that the latter becomes filled with this solution. The proximal Potts clamp is now released and as blood surges into the length of Tygon, it is clamped. Upon assurance that no air is trapped in

the T-tube or tubing, the distal Potts clamp is released and flow restored in the aorta.

Next, the pericardial sac is opened and the left auricular appendage isolated. A purse-string suture is placed in the appendage, and its base occluded with a noncrushing clamp. An incision is made within the area surrounded by the suture and its edges elevated with three small clamps. The auricular drainage tube, with multiple large perforations in its tip, is gently manipulated into the appendage and the purse-string tightened to prevent bleeding. As the clamp is released from the appendage, blood is drawn into this tube with a bulb syringe and the tube clamped so that no air is contained in that portion communicating with the appendage. The tube is advanced further into the auricle and securely tied. The tubing is prepared previously with shallow circumferential grooves in order to keep the suture from slipping. Thus, all pump connections are made with the animal circulation still intact. Unless untoward circumstances, such as a very small or a very friable appendage, are encountered, the procedure is tolerated well by the animal and intravascular pressures are maintained at normal levels.

To connect the animal's circulation to the pump the aortic and left auricular tubings are filled with gelatin solution, care being taken to evacuate all air bubbles. The aortic tubing is connected to the outlet airtrap and the auricular tubing is connected to the pump reservoir (fig. 3). The clamp is removed cautiously from the auricular drainage tube being careful not to permit air to enter the left auricle. When flow into the reservoir has been established, the pump is turned on. At the same instant the clamp is removed from the aortic tube. The left ventricle is now completely removed from the circulation, although it is observed to continue to contract. Initially, the pump rate is usually set at 100 strokes/min. with a stroke volume of 20–25 cc according to the weight of the animal.

Occasionally, as the experimental period begins, the iliac pulse wave is noted to be chaotic. Com-

⁴ Electrothermal heating tapes obtained through E. Machlett & Sons, New York, N. Y.

parison of the iliac tracing with a simultaneous recording of the pressure pulse in the pulmonary artery reveals that the systemic pressure wave is a combination of pressure pulses resulting from pump ejection plus impulses arising from the left ventricle itself. These have been designated 'impure' pressure waves signifying that drainage from the left auricle into the reservoir is not complete so that some blood is passing through the mitral valve and ejected through the aortic valve (fig. 4). Manipulation of the left auricular drainage tube usually resulted in a position being found in which total diversion of left auricular blood could be accomplished without attempting to mechanically close the mitral orifice. When an attempt was made to exclude blood from the left ventricle by inserting a thin rubber balloon into the mitral orifice through a second purse-string in the left auricular appendage, ventricular fibrillation frequently ensued.

There is generally no gross change in intravascular pressures as the extracorporeal circulation begins, except for an occasional transient fall in systemic arterial pressure which soon returns to the previous level. An adjustment period of approximately 10 minutes is permitted to elapse before experiments are begun. During the studies, the chest remains open and covered with warm towels.

RECORDING OF DATA

The systemic arterial and venous pressures are recorded in iliac vessels cannulated with the largest possible diameter polyethylene tubing (approximately 3.0 mm i.d.) or large bore (12 gauge) stain-

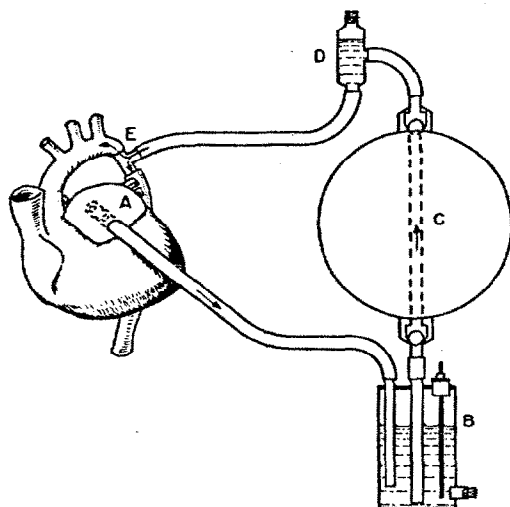


FIG. 3. Diagram of the circuit of blood through the pump. A is a drainage tube in the left auricle; B is the pump reservoir; C is the pump head; D is an air trap; E is the T-tube in the thoracic aorta which allows flow both proximally and distally.

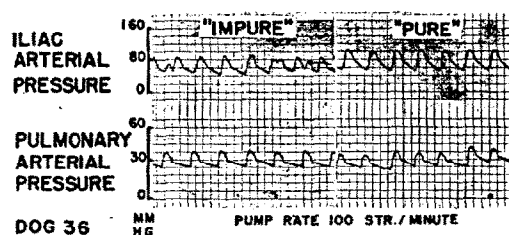


FIG. 4. Cuttings from tracings in dog 36 to show an 'impure' arterial pulse wave 'contaminated' by blood ejected from the left ventricle. The impure components in the systemic arterial pressure pulse contour correspond to right ventricular ejection as indicated by the pulmonary arterial pressure pulse contour. Adjustment of the left auricular drainage tube results in a 'pure' wave, the result of pump ejection alone.

less steel needles. The tubing or needles are coupled directly to strain gages.⁵ Pulmonary arterial pressure is obtained through a smaller diameter catheter placed in a branch of the pulmonary artery. Pressures are recorded simultaneously on a 4-channel direct writing oscillograph⁶ via carrier-wave-type strain gage amplifiers.⁶

Volume flow from the left auricle was obtained in early experiments by directing the total auricular drainage through a de-pulsating air chamber to a Wilson rotameter (9). The rotameter offered a resistance to drainage, especially at low flow rates. Subsequently, timed recordings of reservoir levels have been used to calculate pulmonary blood flow and have proved more accurate than rotameter measurements. An electromagnetic flowmeter⁷ and an acoustic flowmeter (10) have had preliminary trials in the continuous measurement of both left auricular drainage and pump output.

A total of over 36 successful experiments which have varied in duration from 1 to 6 hours have been performed in the course of 3 years. During each procedure several problems under study have been investigated sequentially. Although the purpose of this paper is to present the technique of the study, some of the investigations which have been pursued include the effects of controlled variations in pumping rates and strokes volumes on the peripheral and lesser circulations; the effects of progressive degrees of right ventricular failure including complete right heart failure as in ventricular fibrillation; the effects of drugs which act on various components of the cardiovascular system such as epinephrine, and the relationships between the generation of pressure pulse contours and the velocity and volume of flows in various segments of the cardiovascular system.

⁵ Statham Laboratories, Beverly Hills, Calif.

⁶ Sanborn Company, Cambridge, Mass.

⁷ Mittelman Electronics Corp., Chicago, Ill.

SUMMARY

An experimental method is described in which a hydraulically actuated diaphragm pump is substituted for the left ventricle in dogs. The pump permits independent control of pump rate and stroke volume. Blood is drained from the left auricle and pumped into the descending thoracic aorta both proximally and distally, thus completely bypassing the left ventricle. Detailed descriptions of the apparatus, the surgical techniques and the development of the method are given.

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